

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

59597-D/JPW/AJM/CMR

Serial No.

09/766,344



INFORMATION

(Use several sheets if necessary)

Applicants

Neil T. Parkin and Rainer A. Ziermann

Filing Date

January 19, 2001

Group Art Unit

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
SH	5 7 6 6 8 4 2	6/16/98	Melnick, et al. (Exhibit 1);	435	5	
SH	5 8 3 7 4 6 4	11/17/98	Capon, et al. (Exhibit 2);	435	6	

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

SH	International Search Report for the PCT Application No. PCT/US00/17178, filed June 22, 2000 with the U.S. Receiving Office (Exhibit 3);
	Dreyer GB, et al. (1993) "A Symmetric Inhibitor Binds HIV-1 Protease Asymmetrically" <u>Biochemistry</u> 32:937-947 (Exhibit 4);
	J. Eron, et al., (1995) Preliminary Assessment of 141W94 in Combination with Other Protease Inhibitors", <u>5th Conference on Retroviruses and Opportunistic Infections</u> : 6 (Exhibit 5);
	Hill, A. et al. (1998) "Low frequency of genotypic mutations associated with resistance to AZT and 3TC after combination treatment with indinavar", <u>Int. Conf. AIDS</u> 12:812, (Abstract No. 6) (Exhibit 6);
SH	E.E. Kim, (1995) " Crystal Structure of HIV-1 Protease in Complex with VX-478, a Potent and Orally Bioavailable Inhibitor of the Enzyme", <u>J. Am. Chem. Soc.</u> , 117: 1181-1182 (Exhibit 7);

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SH	Lambert DM, et al. (1992) "Human Immunodeficiency Virus Type 1 Protease Inhibitors Irreversibly Block Infectivity of Purified Virions From Chronically Infected Cells" <u>Anit Microb Agents Chem</u> 36:982-988 (Exhibit 8);
	Brendan A. Larder, et al., (1995) "Potential Mechanism for Sustained Antiretroviral Efficacy of AZT-3TC Combination Therapy", <u>Science</u> , 269: 696-699 (Exhibit 9);
	Janis K. Lazdins, et al., (1997) "In Vitro Effect of α_1 -Acid Glycoprotein on the Anti-Human Immunodeficiency Virus (HIV) Activity of the Inhibitor CGP 61775: A Comparative Study with Other Relevant HIV Protease Inhibitors", <u>J Infec. Dis.</u> , 175: 1063-1070 (Exhibit 10);
	David J. Livingston, et al., (1995) "Weak Binding of VX-478 to Human Plasma Proteins and Implications for Anti-Human Immunodeficiency Virus Therapy", <u>J Infec. Dis.</u> , 172:1238-1245 (Exhibit 11);
SH	Bhuvaneshwari Mahalingam, et al., (1999) "Structural and Kinetic Analysis of Drug Resistant Mutants of HIV Protease", <u>Biochem.</u> , 263: 1-9 (Exhibit 12);

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SH	Miller M, et al. (1989) "Structure of Complex of Synthetic HIV-1 Protease with a Substrate-Based Inhibitor at 2.3 A Resolution" <u>Science</u> 246 :1149-1152 (Exhibit 13);
	Mohri H, et al. (1993) "Quantitation of Zidovudine-Resistant Human Immunodeficiency Virus Type 1 in the Blood of Treated and Untreated Patients", <u>PNAS</u> 90 :25-29 (Exhibit 14);
	Robert L. Murphy, et al., (1999) "Treatment with Amprenavir Alone or Amprenavir with Zidovudine and Lamivudine in Adults with Human Immunodeficiency Virus Infection" <u>J. Infec. Dis.</u> , 179: 808-816 (Exhibit 15);
	Nájera I, et al. (1994) "Natural Occurrence of Drug Resistance Mutations in the Reverse Transcriptase of Human Immunodeficiency Virus Type 1 Isolates", <u>Aids Res Hum Retroviruses</u> 10 :1479-1488, (Exhibit 16);
SH	Nájera I, et al. (1995) "pol Gene Quasispecies of Human Immunodeficiency Virus: Mutations Associated with Drug Resistance in Virus From Patients Undergoing No Drug Therapy", <u>J Virol</u> 69 :23-31, (Exhibit 17);

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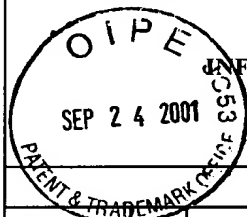
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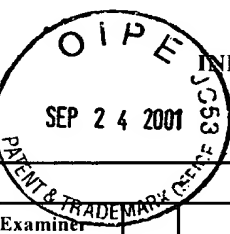
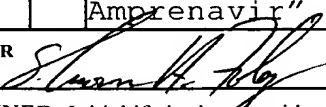
8/2	Roberts NA, et al. (1990) "Rational Design of Peptide-Based HIV Proteinase" <u>Science</u> 248:358-361 (Exhibit 23);
11	Roberts, N. A., (1995) "Drug-resistance patterns of saquinavir and other HIV proteinase inhibitors", <u>AIDS</u> .9 (supp 2) S27-S32 (Exhibit 24);
	Brian M. Sadler, et al., (1999) "Safety and Pharmacokinetics of Amprenavir (141W94), a Human Immunodeficiency Virus (HIV) Type 1 Protease Inhibitor, Following Oral Administration of Single Doses to HIV-Infected Adults", <u>Antimicrobial Agents and Chemotherapy</u> , 43: 1686-1692 (Exhibit 25);
	Sarkar G. and Sommer SS., (1990) "The "Megaprimer" Method of Site-Directed Mutagenesis", <u>BioTech</u> 8(4):404-407 (Exhibit 26);
	Mary L. Smidt, et al., (1996) "A Mutation in Human Immunodeficiency Virus Type 1 Protease at Position 88, Located Outside the Active Site, Confers Resistance to the Hydroxyethylurea Inhibitor SC-55389A", <u>Antimicrobial Agents and Chemotherapy</u> , 41: 515-522 (Exhibit 27);
8/2	M. H. St. Clair, et al., (1996) "In Vitro Antiviral Activity of 141W94 (VX-478) in Combination with Other Antiretroviral Agents", <u>Antiviral Research</u> 29: 53-56 (Exhibit 28);

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SFF		H. Tian, et al., (1998) "Zidovudine/Lamivudine Co-resistance Is Preceded by a Transient Period of Zidovudine Hypersensitivity", 2 nd International Workshop on HIV Drug Resistance and Treatment Strategies, Abstract 30: (Exhibit 29) ;						
/		Tisdåle, M. et al. (1998): "Genotypic and phenotypic analysis of HIV from patients on ZDV/3TC/amprenavir combination therapy", <u>Int. Conf AIDS</u> 12:583 (Abstract No. 32312) (Exhibit 30) ;						
/		Simon P. Tucker, et al., (1998) "Estimate of the Frequency of Human Immunodeficiency Virus Type 1 Protease Inhibitor Resistance Within Unselected Virus Populations In Vitro", <u>Antimicrobial Agents and Chemotherapy</u> , 42: 478-480 (Exhibit 31) ;						
/		Young, B. et al., (1998) "Resistance mutations in protease and reverse transcriptase genes of human immunodeficiency virus type 1 isolates from patients with combination antiretroviral therapy failure. <u>J. Infectious Disease</u> , 178: 1497-1501 (Exhibit 32) ; and						
SFF		Rainer Ziermann, et al., (in press May 2000) "A Mutation in HIV-1 Protease, N-88S, that Causes In Vitro Hypersensitivity to Amprenavir" <u>J Virol.</u> , 74: 4414-4419 (Exhibit 33) .						
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